REMARKS/ARGUMENTS

Reconsideration of the above-identified application, in view of the following remarks, is respectfully requested.

I Status Of The Claims

The Examiner has indicated that claims 26-28 would be allowable if rewritten in independent form including all the limitations of the base claim and any intervening claim. Accordingly, claim 28 has been rewritten in independent form. Claims 26 and 27 have been canceled, and rewritten as new claims 32 and 33, respectively, which depend from claim 28. New claims 32 and 33 are identical to claims 26 and 27, save changes in claim dependency.

New claims 34-36, dependent on claim 28 have been added. Support for the new claims may be found in the specification at page 15, line 30 to page 16, line 18, and in original claims 28-30. No new matter has been added by these amendments.

Claims 14, 15, 19, 24, and 25 have been withdrawn by the Examiner. Claims 1-13, 16-18, 20-23, and 26-36 are currently at issue.

II Rejections under 35 U.S.C. § 112

(i) Claims 1-13, 16-18, 20-23, and 29-31 stand rejected under 35 U.S.C. § 112, first paragraph, for lack of written description. At pages 3-5 of the Office Action, the Examiner quotes from *Regents of the Univ. of Cal. v. Eli Lilly & Co.*, 119 F.3d 1159 (Fed. Cir. 1997) and *Univ. of Rochester v. G. D. Searle & Co., Inc.*, 249 F.2d 216 (W.D.N.Y. 2003). The Examiner asserts that although the specification recites methods for inhibiting PTPases and an assay for determining whether specified candidate inhibitors are suitable, the rejected claims are not limited to specific inhibitor species, but instead recite species characterized incompletely by functionality (such as "interactions" with various enzyme sites) and nominal partial structure (various heterocyclic moieties). The Examiner concludes that the specification represents "no more than a "plan" or

"invitation" to experiment with various partially characterized compounds which might be verified as PTPase inhibitors, without any reasonable expectation of success."

This rejection is respectfully traversed. Contrary to the Examiner's assertion, the specification provides adequate teachings for one skilled in the art to determine which compounds are PTPase inhibitors useful in the claimed methods.

The Examiner quotes the following passage from *Lilly*:

> [i]n claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus.

Lilly at 1568.

This passage simply states that a claim directed to a chemical material which recites a generic formula satisfies the written description requirement. The passage does not state that this is the only way the written description requirement can be satisfied.

Rochester also does not impose any such requirement. The patent at issue in the *Rochester* case has claims directed to a method of selectively inhibiting PGHS-2 activity with a non-steroidal compound that selectively inhibits activity of the PGHS-2 gene product. The patent, however, does not disclose any compounds that can be used in its claimed methods. The Court relied on this fact to establish that the inventors were not in possession of the claimed invention:

> In short, without possession, or at least knowledge, of such compound, or of a method certain to yield such a compound, the inventors could not have possessed the claimed invention, i.e. a method of treatment using the compound.

Rochester at 229.

The Court concluded that:

> The [patent] does not disclose which [compounds] have the desired characteristics of selectively inhibiting PGHS-2. (citation omitted) Without such disclosure, the claimed methods cannot be said to have been described.

Rochester at 224.

Claims 1-13, 16-18, 20-23, and 29-34 of the present application are directed to a method of inhibiting PTPases. Unlike the patent at issue in the *Rochester* case which does not disclose any specific compounds for use in the claimed method, the present application exemplifies **over 100** such compounds (see pages 95-295 of the application) and how they were prepared.

The applicants were, therefore, in possession of compounds which could inhibit the PTPases recited in the claims, and the claimed methods of inhibiting the PTPases.

Contrary to the Examiner's assertion, the application describes structures for the features I-XXXVII recited in the claims. For example, Feature I of claim 1 refers to a phosphate isostere. Page 77 line 28 to page 79, line 5, specifies several such chemical moieties, including $-CH_2PO(OH)_2$, -NHCOCOOH, and $-CONHCF_2COOH$. Feature III of claim 1 refers to a hydrophobic group that interacts with the aromatic ring of tyrosine 46. Page 77, line 23 to page 79, line 9 specifies several examples of hydrophobic moieties, including phenyl, cyclohexyl, and isopropyl.

The Examiner's attention is also drawn to page 50, line 15, to page 51, line 15 of the specification, wherein suitable examples of the hydrophobic and hydrophilic groups that interact with the specific residues on PTB1B are clearly set forth. Moreover, page 51, line 17, to page 62, line 22 of the specification describe how the unique structural elements of PTP1B that act as points of interaction with the PTPase inhibitors were identified, and how the key structural parameters required by PTPase inhibitors that are useful in the claimed methods were optimized for both potency and selectivity.

One of ordinary skill in the art, with reference to pages 50-62 and 77-79 of the specification, would readily appreciate the structural parameters required by PTB1B inhibitors that may be used in the method of the present invention.

As set forth above, the present specification clearly provides adequate teachings of compounds which inhibit PTPase and are useful in the claimed methods. Accordingly, applicants respectfully request that the rejection be withdrawn.

(ii) Claims 1-13, 16-18, 20-23, and 29-31 stand rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement. The Examiner acknowledges that the claims are enabled for the inhibition of PTPases by inhibitors falling within the generic structural formula recited in claim 28, but asserts that the specification "does not reasonably provide enablement for the use of inhibitors as broadly recited by purely functional characteristics."

At pages 2-6 of the Office Action, the Examiner sets forth the *In re Wands* factors, and concludes that the specification would not enable one skilled in the art to practice the invention without undue experimentation. The Examiner states, at page 7 of the Office Action, that the working examples of the specification (as set forth at pages 299-307) "run activity assays on a few select inhibitors, all within the scope of the generic formula set forth in claim 28." The Examiner concludes that the present specification "fails to provide guidance and information sufficient to allow the skilled artisan to ascertain which inhibitors, known of to be discovered, can be used to inhibit PTPases, without resorting to undue experimentation." The Examiner also asserts that "the skilled artisan would expect the interactions of a particular inhibitor and enzyme to be very specific and highly unpredictable, with no *a priori* expectation of success for using specific inhibitors beyond the scope of the generic formula set forth in claim 28."

This rejection is respectfully traversed. Contrary to the Examiner's assertion, the specification provides adequate teachings for one skilled in the art to practice the claimed invention.

The present claims are directed to a method of inhibiting intracellular or membrane-associated PTPases having an aspartic acid (Asp) in position 48 using the numbering for PTP1B, by

exposing the PTPase to an inhibitor compound that possesses certain structural, physico-chemical and spatial characteristics. The Examiner asserts that the claims are very broad and inclusive of inhibitors characterized incompletely by functionality and nominal partial structure.

Contrary to the Examiner's assertion, as set forth above, these structural and spatial characteristics of suitable inhibitor compounds useful in the present invention are described at pages 50-62 and 77-79 of the present specification. One skilled in the art could easily and readily determine what compounds fall within the scope of the claims and necessarily possess the features recited therein.

According to the current law and patent practice, the specification can permit some inferences to be drawn by those skilled in the art, and still comply with the enablement and written description requirements. In other words, there is no requirement that the claims be restricted to the working examples. Section 2164.03 of MPEP recites:

> the scope of the required enablement varies inversely with the degree of predictability involved, but even in unpredictable arts, a disclosure of every operable species is not required (*In re Vaeck*, 947 F.2d 488, 496 & n.23, 20 USPQ2d 1438, 1445 & n.23 (Fed. Cir., 1991); *In re Vickers*, 141 F.2d 522, 526-27, 61 USPQ 122, 127 (CCPA 1944); *In re Cook*, 439 F.2d 730, 734, 169 USPQ 298, 301 (CCPA 1971))

As further stated in section 2164.08 of MPEP:

> claims are not rejected as broader than the enabling disclosure under 35 U.S.C. 112 for non-inclusion of limitations dealing with factors which must be presumed to be within the level of ordinary skill in the art; the claims need not recite such factors where one of ordinary skill in the art to whom the specification and claims are directed would consider them obvious (*In re Skrivan*, 427 F.2d 801, 806, 166 USPQ 85, 88 (CCPA 1970))... When analyzing the enabled scope of a claim, the teachings of the specification must not be ignored because claims are to be given their broadest reasonable interpretation that is consistent with the specification.

See also *Application of Angstadt* (537 F.2d 498, 502-503, 190 USPQ 214, 218 [Cust. & Pat.App., 1976]) stating that applicants "are not required to disclose every species encompassed by their claims even in an unpredictable art." Similarly, in *In re Rasmussen*, court stated that "a claim

may be broader than the specific embodiment disclosed in a specification" (650 F.2d 1212, 1215, 211 USPQ 323, 326 [Cust. & Pat.App., 1981]). Finally, in *In re Goffe* (542 F.2d 564, 567, 191 USPQ 429, 431 [CCPA 1976]), the court stated:

> To provide effective incentives, claims must adequately protect inventors. To demand that the first to disclose shall limit his claims to what he has found will work or to materials which meet the guidelines specified for "preferred" materials in a process such as the one herein involved would not serve the constitutional purpose of promoting progress in the useful arts.

One of ordinary skill in the art would readily recognize those conditions, such as autoimmune diseases, acute and chronic inflammation, osteoporosis, cancers, type I diabetes, type II diabetes, and obesity, in which the substrates identified in the specification are involved. Indeed, the present specification discloses numerous references that teach various conditions that are associated with PTPases (see "Summary Of Background Section" on pages 15-16 of the present specification).

Applicants need not provide working examples for all embodiments of the invention. The Examiner, moreover, has mis-characterized the level of guidance present in the instant specification, overstated the amount of experimentation required to determine specific PTPase inhibitors and underestimated the level of skill in the art.

Accordingly, in view of the arguments set forth above, applicants believe that the pending claims in this application are fully enabled by the specification, and respectfully request that this rejection be withdrawn.

In view of the foregoing remarks, each of the presently pending claims in this application is believed to be in condition for allowance. Accordingly, the Examiner is respectfully requested to pass this application to issue.

Dated: August 2, 2004

Respectfully submitted,

By _____

Jonathan P. Mitchell, Ph.D.
Registration No.: 50,239
DARBY & DARBY P.C.
P.O. Box 5257
New York, New York 10150-5257
(212) 527-7700
(212) 753-6237 (Fax)
Attorneys/Agents For Applicant